Malignant or Accelerated Hypertension

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Malignant or accelerated hypertension is a life-threatening medical emergency that is a possible complication of practically any hypertensive disorder. If not promptly treated it can cause severe, rapidly progressive target-organ damage and death. While the histopathologic features of malignant hypertension are well recognized, the pathogenesis of the associated vascular lesions and the transition from a benign to a malignant phase are unclear. With adequate control of hypertension, progression to the accelerated or malignant phase can be prevented. Moreover, promptly and effectively reducing the blood pressure during the malignant phase can prevent, minimize or even reverse serious target organ injury. Malignant hypertension, therefore, is both preventable and treatable.

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Malignant or accelerated hypertension is diagnosed when there are severe diastolic hypertension usually exceeding 120 to 140 mm of mercury and one or more of the following conditions:

- hypertensive retinopathy with papilledema;
- hypertensive encephalopathy;
- renal involvement;
- acute left ventricular dysfunction—that is, left ventricular failure, pulmonary edema, angina pectoris or myocardial infarction.

In addition, microangiopathic hemolysis, weight loss, anorexia, malaise, debility and fever commonly accompany this syndrome. Polydipsia also occurs with considerable frequency and may be due to either hypovolemia or a dipsogenic effect of raised angiotensin levels, or both.[1]

The term "accelerated hypertension" is often used when symptoms and signs of malignant hypertension occur without papilledema. In this communication, however, the two terms are used interchangeably.

Incidence and Prognosis

Malignant hypertension can complicate the course of practically all forms of hypertension and as such should be regarded as a phase in the course of hypertensive disorders. Successful control of hypertension, irrespective of cause, can greatly reduce or eliminate the occurrence of the malignant phase. The transition from a benign to a malignant phase in patients with essential hypertension takes an average of 7.7 years, ranging from 1 to 30 years.[2(pp134-135)] Before the advent of effective antihypertensive agents, 6% to 8% of cases of hypertension progressed to a malignant or accelerated phase; since then the incidence has declined to about 1%. In fact, occurrence of the malignant phase in patients receiving regular antihypertensive therapy is exceedingly rare. The peak incidence of the malignant phase occurs in middle-aged patients. It is more prevalent in men than in women and more common in American blacks than in whites.

With regard to prognosis, the one- and five-year survival is 20% and 0%, respectively, in untreated persons.[3] With early and vigorous treatment, however, the one- and five-year survival has increased to 85% and 60%, respectively.[4] It should be noted that the chance for survival is lower in patients who have renal insufficiency, with one- and five-year survival being 55% and 25%, respectively.[4,5]

Etiology

The single most common cause of malignant hypertension (40%) is essential hypertension, particularly when untreated or inadequately controlled. Chronic interstitial nephropathy and chronic glomerulonephritis also commonly predispose to malignant hypertension.

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Other, less prevalent, predisposing conditions include polyarteritis nodosa, unilateral renal artery stenosis, postpartum hypertension, eclampsia, radiation nephritis, congenital renal disorders, hydronephrosis, pheochromocytoma, renal thromboembolic phenomena, scleroderma, Cushing's syndrome, primary aldosteronism, renal tuberculosis and the use of estrogen and oral contraceptive agents.[6-20] Occasionally malignant hypertension occurs—primarily in young black men—when there is no preexisting hypertension or known predisposing disorders.[21]

Pathogenesis

The pathogenesis of malignant hypertension has not been fully elucidated. Several mechanisms have been proposed as possible causes of the vascular lesions in malignant hypertension and the transition from a benign to a malignant phase.

Role of Elevated Blood Pressure

Some authors believe that severe hypertension per se is responsible for the genesis of a characteristic fibrinoid arteriolar lesion in malignant hypertension.[22,23] This viewpoint is based on the following observations: (1) malignant hypertension can complicate the course of hypertensive disorders of diverse etiology, (2) vascular lesions have been shown to correlate with the severity of hypertension in humans[23] and in experimental animals,[24] (3) vascular lesions can rapidly resolve with adequate control of hypertension,[24,25] (4) when hypertension is produced in one of a pair of parabiotic rats, only the hypertensive rat will have fibrinoid arteriolar lesions[26] and (5) necrotizing arteriolitis can occur in a pulmonary vascular bed in patients who have severe pulmonary hypertension with normal arterial blood pressure.[27,28]

Role of the Renin-Angiotensin System

The possible role of the renin-angiotensin system in the genesis of vascular lesions of malignant hypertension has been suggested by the following observations: (1) plasma concentrations of renin[29] and angiotensin[30,31] are greatly elevated in almost all patients with malignant hypertension, (2) vascular lesions similar to those seen in malignant hypertension can be produced by the administration of crude kidney extract[32,33] and renin preparations in animals that have had nephrectomies[34] and (3) angiotensin infusion can produce similar lesions in experimental animals.[35,36]

It should be noted, however, that malignant hypertension and associated vascular lesions can occur in the absence of hyperreninemia. For instance, vascular lesions similar to those observed in malignant hypertension can be produced in nephrectomized animals using various pressor agents including vasopressin and catecholamines.[37-39] In addition, fibrinoid arteriolar lesions can be produced in animals by clamping a renal artery both with contralateral nephrectomy (low renin) and without contralateral nephrectomy (high renin), provided the resultant hypertension is sufficiently severe.[40-42] Moreover, Thiel and co-workers have shown that hypertensive vascular lesions in a deoxycorticosterone-induced low-renin model can be more severe than those observed in a high-renin model induced in experimental animals by clamping a renal artery.[43] Finally, a malignant phase does, rarely, occur in cases of primary hyperaldosteronism, a condition in which the renin-angiotensin system is suppressed.

Role of Disseminated Intravascular Coagulation

The common association of microangiopathic hemolysis and intravascular coagulation with malignant hypertension is well established. To date, it is not clear whether malignant hypertension is the cause or the effect of this process. It is thought that the vascular changes contribute to the occurrence of intravascular coagulation and hemolytic anemia with erythrocyte fragmentation.[44] At times, however, hemolytic anemia precedes the onset of hypertension.[45] Linton and associates have suggested that elevated blood pressure in malignant hypertension results in alteration of permeability characteristics of small arteries and accumulation of fibrinogen in the wall of these arterioles.[46] This, in turn, causes microangiopathic hemolysis and disseminated intravascular coagulation, thereby perpetuating the associated vasculopathy.

Role of a Negative Sodium Balance

The role of sodium balance in the genesis of the malignant phase of hypertension is not fully recognized. Interestingly, however, experimental malignant hypertension is associated with increased urinary sodium excretion and negative sodium balance.[47,48] The weight loss commonly seen during the acute phase of malignant hypertension may be due to this negative salt and water balance. It has been suggested that the initial loss of sodium and the resultant activation of the renin-angiotensin system may trigger the vicious cycle leading to the malignant phase and associated vascular lesions. The underlying mechanism responsible for the initial naturesis in malignant hypertension is not clear, though alteration of renal hemodynamics has been suggested.[49]

Malignant Nephrosclerosis

When uncontrolled, malignant hypertension often results in a rapidly progressive renal lesion called malignant nephrosclerosis. With prompt and effective treatment, however, renal damage can be prevented or reversed.[3,25]

The gross appearance and size of a kidney during the acute phase depend on the nature and duration of the underlying renal disease. For instance, small contracted kidneys are seen with preexisting benign nephrosclerosis, large scars with chronic pyelonephritis and normal-sized kidneys in de novo malignant nephrosclerosis. Petechial hemorrhages on the surface of the kidneys due to rupture of arterioles give the kidneys a flea-

bitten appearance. The histologic findings may be difficult to distinguish from those associated with scleroderma and adult hemolytic-uremic syndrome. These lesions consist of three major changes:

1. Proliferative Endarteritis

Proliferative endarteritis involves the interlobular arterioles and gives rise to a so-called onion-peel appearance. It is thought to be due to fibroblastic proliferation of subendothelial connective tissue, which results in severe narrowing or obliteration of arteriolar lumina. The pronounced arteriolar narrowing or obliteration in turn causes renal parenchymal ischemia and necrosis. This lesion, which can develop with great rapidity, is regarded by some to be highly specific for malignant hypertension. The thickened intima consists of mucoid material and thin concentric layers of collagen separated by elongated fibroblasts. These cells are thought to represent modified smooth muscle cells migrating from the media through disrupted internal elastic lamina. The ground substance appears to be acidic mucopolysaccharide similar to that seen in systemic sclerosis.[50] In addition, macrophages containing lipid droplets may be present in the thickened intima of the affected arterioles.

2. Necrotizing Arteriolitis

Necrotizing arteriolitis is characterized by fibrinoid necrosis of the afferent arterioles. In contrast to vasculitides, inflammatory cells are usually absent from the wall of the affected vessels. Intratubular and parenchymal hemorrhages, however, often occur due to disruption of the vessels. Because the finely granular eosinophilic substance found in these lesions shows staining properties of fibrin, it is referred to as fibrinoid. On immunofluorescence microscopy the material is reactive not only with antisera against fibrinogen but also with antisera against other plasma proteins including albumin, immunoglobulins and C3.[51] These changes are usually accompanied by cellular necrosis. Many authors consider necrotizing arteriolitis to be characteristic of malignant hypertension.

3. Necrotizing Glomerulitis

Necrotizing glomerulitis is characterized by fibrinoid necrosis and polymorphonuclear leukocyte infiltration of the glomeruli, whose afferent arterioles show necrotizing arteriolitis. In addition, other ischemic changes are often present, including shrinkage of the glomerular tuft and wrinkling of the basement membrane. These glomerular changes may progress to cellular proliferation that mimics chronic glomerulonephritis. The irregular and focal pattern of the glomerular involvement in malignant nephrosclerosis (rarely affecting more than a third of glomeruli) differentiates it from diffuse proliferative glomerulonephritis, which shows a widespread distribution. Occasionally extracapillary proliferation with crescent formation is seen.[52] Immunofluorescence microscopy usually shows the presence of plasma proteins, particularly fibrin, in the areas of fibrinoid necrosis and the intimal lesions of the involved arterioles.[2(pp146-148),53,54] Pathologic changes associated with underlying disorders, when present, are also seen. With prompt and effective control of hypertension the acute vascular and glomerular lesions usually regress with or without some residual scars.[3,5,25] Long-term follow-ups, however, have shown that in larger arteries that are unaffected, during the acute phase moderate to severe subintimal fibrous hyperplasia frequently develops.[5] The resultant ischemia can produce a later reduction of renal function. Partial recovery of renal function has been reported in some patients with severe renal failure after several days to several months of dialysis therapy and hypertension control.[55,56] Potential reversibility of renal lesions with blood pressure control has also been documented in both patients and experimental animals with malignant nephrosclerosis.[24,57] Renal arteriography usually shows abnormal intrarenal vasculature and irregularity of the walls of interlobar and interlobular arteries and a diminished and patchy appearance on a nephrogram.

Proliferative endarteritis and necrotizing arteriolitis may occur in other organs besides the kidney, such as the central nervous system, gastrointestinal tract, pancreas, liver and adrenal glands.

Clinical and laboratory manifestations of malignant nephrosclerosis consist of proteinuria, microscopic or gross hematuria,[58] cylindruria, oliguria and progressive azotemia. These urinary abnormalities and the associated hypertension with or without azotemia may mimic an acute nephritic or vasculitic process. However, hypertension tends to be less severe in those conditions, a history of preexisting hypertension is often lacking and urinary abnormalities and other related manifestations usually precede the onset of hypertension. Nevertheless, the differentiation is occasionally difficult and requires renal biopsy. Irrespective of the underlying disorder, rapid control of hypertension is indicated.

Hematologic Abnormalities

Hematologic abnormalities include changes of the coagulation and fibrinolytic systems and microangiopathic hemolysis. The associated microangiopathic hemolytic anemia may be initially masked by hemoconcentration, which frequently accompanies the acute phase of accelerated hypertension. Often a significant fall in the hematocrit is subsequently noted, representing the reversal of hemoconcentration with or without hemolysis and renal failure. The main coagulation abnormalities include thrombocytopenia, increased fibrin-degradation products and increased factor VIII and fibrinogen concentrations. In addition, increased sensitivity to urokinase and decreased euglobulin lysis time may be noted.[59] Increased erythrocyte sedimentation rate[60] and elevated serum IgG concentration are also seen.[19]

Endocrinologic Changes

As mentioned earlier, malignant hypertension is usually associated with intense stimulation of the renin-

angiotensin-aldosterone system. This is evidenced by pronounced elevation of serum levels of renin, angiotensinogen, angiotensin II and aldosterone. Intense stimulation of this system may be due either to the negative sodium and fluid balance or to pathologic changes involving the juxtaglomerular apparatus (or to both). These changes occasionally do not occur. Hypokalemia and alkalosis are often noted in cases of malignant hypertension and represent the effects of increased aldosterone levels on renal electrolyte handling. Due to intense adrenal stimulation, aldosterone overproduction and associated electrolyte abnormalities may persist long after the reversal of volume contraction and return of the renin level to or below normal limits. This condition should not be mistaken for primary hyperaldosteronism. Abnormal stimulation of the antidiuretic hormone has also been reported in both humans and animals with experimentally induced malignant hypertension.[61,62]

Hypertensive Encephalopathy

Hypertensive encephalopathy is one of the most serious manifestations of malignant or accelerated hypertension. Its clinical picture consists of a wide spectrum of neurologic aberrations that develop acutely as a result of severe hypertension.[63] The symptoms and signs vary from severe headache, nausea, vomiting, blurred vision and confusion to transient blindness, paralysis, seizures, stupor and deep coma. Occasionally focal neurologic deficits can also develop; however, they are uncommon and should suggest other central nervous system disorders. As a result of pronounced cerebral edema, fatal cerebellar herniation may occur. This event may be facilitated or induced by lumbar puncture. In most cases the cerebrospinal fluid pressure and protein concentration are raised. Neurologic features are sometimes reversed within a few days following control of hypertension, but at times recovery is slow or incomplete. Pathologic findings include arteriolar wall thickening and necrosis, cerebral edema and areas of hemorrhage.

Hypertensive encephalopathy may be clinically simulated by other neurologic disorders such as intracerebral or subarachnoid hemorrhage, thrombotic stroke or metabolic encephalopathy such as that associated with uremia. In these and other conditions associated with intracranial hypertension, retinal hemorrhage, papilledema and arterial hypertension can occur. Consequently cause or effect relationship with hypertension may be difficult to ascertain. Arterial hypertension is usually less severe with a primary intracranial pathologic condition, focal neurologic deficits are more distinct and appear earlier in the course and central nervous system manifestations generally persist despite hypertension control. Controversy exists regarding the rapidity with which the blood pressure should be lowered in patients with hypertensive encephalopathy. Some authorities regard a prompt return of the blood pressure to a normal level as safe.[64,65] Others believe, however, that rapid reduction of blood pressure may cause irreversible ischemic brain damage and recommend a less drastic approach.[66,67]

Retinopathy

Involvement of retinal arterioles leads to obliteration or rupture of these vessels, or both. This will result in the development of certain funduscopic lesions including fluffy cotton-wool exudates representing ischemic injury to the nerve fibers, flame-shaped hemorrhages due to rupture of blood vessels and papilledema associated with intracranial hypertension. The associated symptoms include blurred vision, a narrowed visual field, transient loss of vision, scotomas and the like.

Preventing Malignant Hypertension

According to the results of the Veterans Administration's cooperative study on essential hypertension, medical management of patients reduced the incidence of congestive heart failure, hypertensive retinopathy and kidney failure.[68] In this study malignant hypertension did not develop in any of the treated patients, suggesting that it is preventable. Although controlled studies of the effect of antihypertensive therapy in patients who have renal hypertension are lacking, a similar result can probably be expected.

Treatment

The diagnosis of malignant hypertension mandates immediate admission to hospital and institution of effective antihypertensive therapy. The latter should not be delayed because of diagnostic evaluations. These measures should either be deferred or conducted concurrently with the treatment.

The prompt use of potent antihypertensive drugs is the mainstay in the treatment of malignant hypertension. The immediate aim of the treatment should be to reduce the diastolic blood pressure to about 90 to 105 mm of mercury within a few hours. Caution should be exercised in patients with advanced arteriosclerosis who may fail to maintain adequate blood flow to the vital organs following a rapid fall in blood pressure. Because this can cause thrombosis or ischemic damage, particularly in the central nervous system, rapid reduction of diastolic blood pressure below 100 mm of mercury may be undesirable (see section on encephalopathy). The initial fall in tissue perfusion following blood pressure control in cases of malignant hypertension is best illustrated by the common occurrence of a transient increase in plasma creatinine and urea concentrations.

Oral medication can be initiated concurrently with, or anytime after, the initiation of emergency parenteral therapy. The dose of oral agents should be titrated to produce the desired blood pressure without the use of parenteral agents. The use of diuretics during the acute phase depends on the sodium and fluid balance. Due to the known negative sodium balance and intravascular fluid contraction during the acute phase of malignant hypertension, the use of diuretics initially is not warranted. Later, however, diuretics may be necessary as fluid retention becomes evident. In addition, diuretic

therapy can be instituted at the time of presentation in a few patients who have evidence of sodium excess and fluid overload. The argument against the initial use of diuretics in cases of malignant hypertension is strengthened by the reported successful treatment of this condition with saline infusion.[69,70] A brief discussion of the mechanisms of action, indications, contraindications, routes of administration and side effects of the drugs used in the acute phase of malignant hypertension follows.

Diazoxide

Diazoxide is a benzothiadiazine derivative that structurally resembles thiazide diuretics but lacks diuretic effect. It is a potent arteriolar smooth muscle relaxant but has no effect on the capacitant vessels and arterial baroreceptors. Consequently, its hypotensive effect is associated with tachycardia and increased cardiac output. The latter effects can lead to angina pectoris and even myocardial infarction in the presence of coronary artery insufficiency. While the exact subcellular mechanism of diazoxide's action remains uncertain, it is believed to be due to either depletion of the intracellular calcium (Ca^{++}) pool or the blockade of Ca^{++} release or Ca^{++} receptors.

When injected intravenously, diazoxide usually produces a prompt fall in blood pressure within a minute, reaching its maximum effect within two to five minutes with the effect lasting 3 to 15 hours. The conventional dose of diazoxide is 5 mg per kg of body weight in children and 300 mg in adults rapidly given intravenously. If not effective the dose can be repeated 30 minutes later.

While highly effective in rapidly lowering blood pressure, the use of a standard dose of diazoxide can be associated with serious consequences including severe hypotension, stroke, angina pectoris, myocardial infarction and even death.[71-73] Slow intravenous infusion of diazoxide has recently been shown to be effective in controlling severe hypertension.[74] In addition, small doses of diazoxide (100 to 150 mg) given intravenously (miniboluses) have been effective and relatively free of the serious complications.[75] The dose can be repeated every five minutes until the desired blood pressure is attained. Irrespective of the mode of administration, the use of diazoxide in patients with coronary artery insufficiency requires concomitant administration of a β-blocker to prevent myocardial ischemia.

In addition to the major side effects mentioned earlier, diazoxide can lead to hyperglycemia (inhibition of insulin secretion), potentiation of the coumarin effect (competition for protein binding sites), hyperuricemia, fluid retention and the arrest of labor in pregnant patients (relaxation of uterine smooth muscle). This last effect can be reversed by administering oxytocin.

Sodium Nitroprusside

Sodium nitroprusside is one of the most effective antihypertensive agents presently available. Its only route of administration is intravenous. It is a direct vasodilator that, unlike diazoxide and hydralazine, affects both arterial and venous systems. It can, therefore, reduce cardiac output and readily cause extreme hypotension. Due to the reduction of both preload and afterload, it may ameliorate the associated heart failure. The drug is available as a sterile powder, which is usually dissolved in 5% dextrose in water and slowly infused intravenously. The usual starting dose is 0.2 to 0.5 μg per kg per minute and can be increased to a maximum of 8 μg per kg per minute. The rate of infusion is determined and adjusted by careful and frequent blood pressure monitoring. Continuous blood pressure monitoring through an arterial line is highly desirable. The onset and duration of the action of nitroprusside is one and three to four minutes, respectively, with the peak effect occurring between one and two minutes. It consistently lowers the blood pressure in most patients, even those resistant to other drugs. Its use does not result in tachyphylaxis (drug resistance). When in a solution, it is inactivated upon exposure to light, so the bottle and the tubings should be covered to prevent inactivation. Prolonged use of this drug (more than 48 hours) especially at high doses can lead to thiocyanate toxicity. This is due to the generation of cyanide in tissues, which is rapidly converted to thiocyanate. When the plasma thiocyanate level exceeds 10 to 12 mg per dl, weakness, nausea, tinnitus, dizziness, hypothyroidism and even psychosis can develop. A thiocyanate toxic reaction can occur more readily in patients with renal failure due to its reduced renal excretion. Intermittent hemodialysis is effective in removing this substance and alleviating the associated symptoms. The blood thiocyanate level should be measured periodically in patients receiving nitroprusside. A reversible hypothyroidism can occur with prolonged nitroprusside treatment. Following withdrawal of nitroprusside, the thyroid function returns to normal spontaneously.

Hydralazine Hydrochloride

Hydralazine hydrochloride is a potent antihypertensive drug that causes vasodilation by direct effect on the smooth muscles of the arterioles. Reflex tachycardia, throbbing headache and a lupuslike syndrome are among its major side effects. Because of reflex tachycardia, myocardial oxygen consumption increases with this drug. Angina and myocardial infarction may develop in patients with ischemic heart disease if tachycardia is not controlled. Simultaneous use of β-blockers not only counteracts this effect, but also potentiates the antihypertensive action of hydralazine. It is, therefore, necessary to use β-blockers in conjunction with hydralazine in such patients. Intramuscular or intravenous injection of hydralazine in doses of 5 to 30 mg every four to six hours is frequently adequate for controlling malignant hypertension in most patients. In large doses hydralazine can cause agitation and anxiety, which may be confused with symptoms of hypertensive encephalopathy. If after two hours the blood pressure cannot

be controlled with parenteral hydralazine, another agent should be used.

Trimethaphan Camsylate

Trimethaphan camsylate and other ganglionic blocking agents exert their antihypertensive action by competitive inhibition of acetylcholine in sympathetic ganglia, thus preventing postsynaptic depolarization. With slow intravenous infusion, trimethaphan camsylate exerts a potent blood pressure-lowering action that is potentiated by postural effects. The need for constant monitoring of blood pressure, parasympatholytic side effects—that is, dry mouth, urinary retention, visual impairment associated with cycloplegia, tachycardia, constipation and ileus—and the development of resistance to the drug are among its major disadvantages.

Reserpine

By depleting the postganglionic catecholamine stores, reserpine and other *Rauwolfia* preparations interfere with adrenergic neurotransmission and thereby reduce peripheral vascular resistance. Reserpine can be administered intramuscularly in doses of 1.0 to 2.5 mg in a hypertensive crisis. There is usually a delay of 1½ to 2½ hours (sometimes 8 hours) in the onset of its action, which lasts about 7½ to 8 hours. A delayed and unpredictable response and various side effects (mainly nasal congestion, peptic disorders and central nervous system depression) are among the disadvantages of the use of this drug.

Clonidine Hydrochloride

Clonidine hydrochloride is a centrally acting α-agonist whose usefulness in the long-term management of hypertension is well established. Intramuscular injection of clonidine in a dose of 150 μg can produce a hypotensive response within 30 minutes that lasts four to six hours. If necessary, the dose may be repeated after 60 minutes. Unlike diazoxide and hydralazine, clonidine does not increase the heart rate and cardiac output. It is, therefore, safer in patients who have ischemic heart disease than the former agents. When given intravenously, clonidine may transiently augment the hypertension due to its weak α-agonistic property. The initial dose should therefore not be given intravenously, but this route can be used subsequently without added risk. It should be noted that clonidine has a sedative effect that can complicate the assessment of the associated encephalopathy. Oral administration of clonidine should be initiated concurrently with parenteral dosing to allow discontinuation of the latter and the maintenance of hypertension control.

The oral administration of clonidine for rapid titration of blood pressure in cases of severe hypertension has recently been advocated by several investigators.[72-78] Using rapid titration with oral clonidine, Spitalewitz and co-workers[76] were able to effectively lower the blood pressure in 20 patients with severe hypertension. They administered 0.2 mg of clonidine as the initial dose followed by 0.1 to 0.2 mg at one hour and 0.1 mg hourly thereafter as necessary (not to exceed 0.8 mg). The blood pressure fell from 212 ± 7/134 ± 3 mm of mercury on presentation to 151 ± 5/104 ± 3 mm of mercury within about two hours. The average cumulative dose producing the desired response was 0.32 ± 0.02 mg. Most of the patients were treated in an emergency room as outpatients and only a few were admitted to hospital. The results of these studies suggest that rapid titration with oral clonidine is effective in controlling severe hypertension. This approach may be inadequate, however, in treating patients who have florid malignant hypertension; such patients should receive rapidly acting potent parenteral agents under close observation.

With the use of one of the above modalities, the blood pressure should be promptly lowered to a safe level. When possible, the use of oral agents should be initiated with the onset of parenteral therapy or shortly thereafter to allow gradual reduction and discontinuation of the parenteral drugs. Heparin and dipyridamole have been recommended by some investigators to limit the associated microangiopathic hemolysis and intravascular coagulation.[79,80] Due to their potential risks and uncertain usefulness, however, the use of anticoagulants in such patients is not recommended at this time.

Dialysis

Renal failure with associated uremia is a common complication of malignant hypertension. In the predialysis era 95% of the mortality in cases of malignant hypertension was caused by uremia. In addition to its lifesaving value, dialysis can serve as a diagnostic tool to differentiate the metabolic form from the hypertensive form of encephalopathy. Furthermore, because fluid overload associated with renal insufficiency can contribute to hypertension, fluid removal by dialysis can facilitate blood pressure control in a case of malignant hypertension.

Role of Surgery and Nephrectomy

A few patients in whom malignant hypertension is associated with surgically correctable lesions, such as with renal artery stenosis, primary hyperaldosteronism or coarctation of the aorta, will benefit from the surgical correction of the lesion.

Bilateral nephrectomy in patients who have malignant hypertension results in a dramatic reduction of the hypertension. This procedure has been used in the past for the management of certain patients with intractable malignant hypertension. With the availability of potent antihypertensive agents, however, nephrectomy no longer has a place in the treatment of this disorder. Even in the presence of irreversible renal failure, this procedure should be avoided when possible, due to the added difficulties with anemia, bone disease and fluid and electrolyte disorders associated with an anephric state.[81] Moreover, partial recovery of renal function may occur, obviating the need for dialysis in some patients months after the initiation of

dialysis.[55,56] A small subgroup of dialysis patients with severe hypertension have severe hyperreninemia, pronounced volume-independent hypertension, anorexia, weight loss and progressive deterioration of their general condition. Bilateral nephrectomy may be indicated in such patients.[82] The procedure may also be rarely indicated in the treatment and prevention of severe hypertension in renal transplant recipients.[83]

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Medical Practice Questions

EDITOR'S NOTE: *From time to time medical practice questions from organizations with a legitimate interest in the information are referred to the Scientific Board by the Quality Care Review Commission of the California Medical Association. The opinions offered are based on training, experience and literature reviewed by specialists. These opinions are, however, informational only and should not be interpreted as directives, instructions or policy statements.*

Continuous Passive Motion for Joint Mobilization

QUESTION:

Is it considered acceptable medical practice to use continuous passive motion as a routine standard procedure in the postoperative management of stiffening conditions?

OPINION:

In the opinion of the Scientific Advisory Panels on General Surgery, Orthopedics and Physical Medicine and Rehabilitation, continuous passive motion is considered established practice in the postoperative management of stiffening conditions associated with total knee or total hip replacement and muscle and joint release surgical procedures. Additional indications include intraarticular fracture operations of the knee, hip, elbow and shoulder.

Use of continuous passive motion has been shown to reduce postoperative swelling and pain, and to improve range of motion in patients who have undergone the surgical procedures noted.

Continuous passive motion is also an accepted modality of treatment for intraarticular fractures and stiffening conditions.